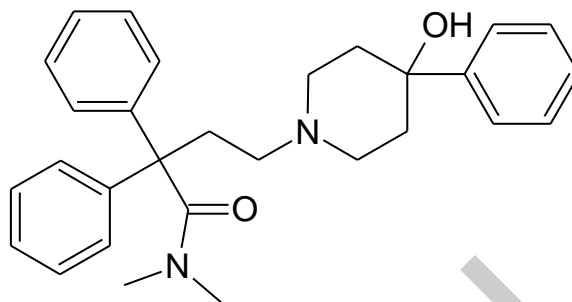


Reference Material Product Information Sheet

Epichem's Quality System conforms to ISO9001:2015 as certified by ECAAS Pty Ltd - Certification number 616061.



Name	4-(4-hydroxy-4-phenylpiperidin-1-yl)- <i>N,N</i> -dimethyl-2,2-diphenylbutanamide
BP/EP Name	Loperamide Impurity D
USP Name	Not listed.
Epichem Item #	EPL-AA158 Batch 1
CAS #	37743-41-2
Molecular Formula	C ₂₉ H ₃₄ N ₂ O ₂
Molecular Weight	442.61 g/mol
Appearance	White powder
Melting Point	81.6-100.6°C
Combustion Analysis	Required (%): C:78.7; H:7.7; N:6.3. Found (%): C:78.7; H:7.8; N:6.3.
Purity*	99.0%
Date of Manufacture	2 December 2014
Storage Requirements	Protect from heat, light and moisture.
Special Precautions	This compound is for laboratory use only. Its toxicological properties may not have been fully established. It should be handled only by suitably qualified personnel.
Intended Use	This compound is suitable for the identification of impurities and degradants in pharmaceutical materials. The purity assay is considered as relative contribution.
Date of Shipment	TBA
	This certificate is valid for one year from the date of shipment provided the substance is stored under the recommended conditions.
Retest Date	TBA (Proper Storage and Handling Required)

* NATA accreditation does not cover the performance of this service

EPL-AA158 Batch 1

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I. Identity

The identity of this product was established using the following analyses:

Ia. ¹HNMR Spectrum

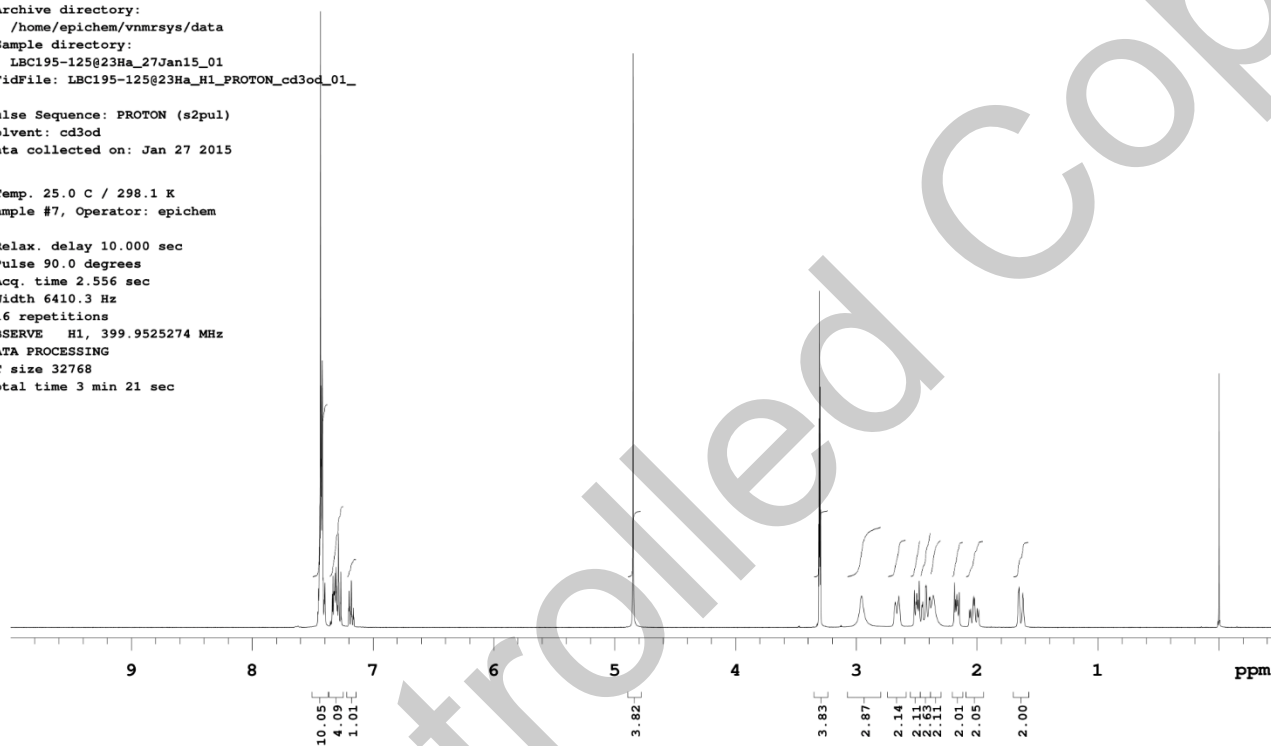
Conditions: 400 MHz, CDCl₃
¹HNMR spectrum consistent with chemical structure.

```
Sample Name:
LBC195-125@23Ha
Data Collected on:
nmronline.murdoch.edu.au-vnmrs400
Archive directory:
/home/epichem/vnmrsys/data
Sample directory:
LBC195-125@23Ha_27Jan15_01
FidFile: LBC195-125@23Ha_H1_PROTON_cd3oc_01_

Pulse Sequence: PROTON (s2pul)
Solvent: cd3oc
Data collected on: Jan 27 2015

Temp. 25.0 C / 298.1 K
Sample #7, Operator: epichem

Relax. delay 10.000 sec
Pulse 90.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
16 repetitions
OBSERVE H1, 399.9525274 MHz
DATA PROCESSING
FT size 32768
Total time 3 min 21 sec
```



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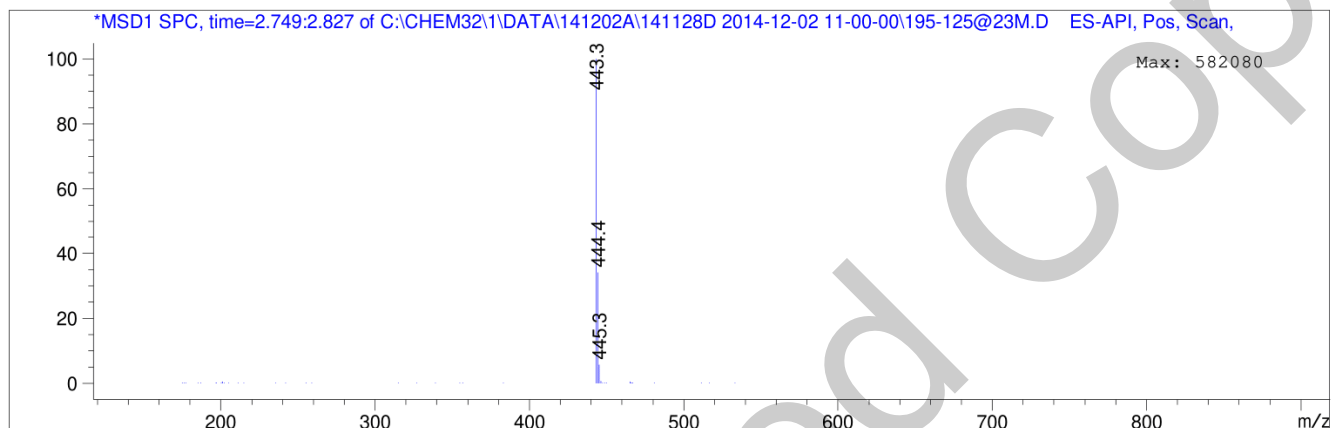
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Ib. Mass Spectrum

The mass spectrum of this material was analysed by Liquid Chromatography Mass Spectroscopy (LCMS) using in-house EM005.WI08.

Method: 5% to 100% ACN in water gradient (+0.1% formic acid)

Retention Time (MS)	MS Area	Mol. Weight or Ion
2.780	5889929	444.35 443.30



Theoretical value: 443.3 [M+H]⁺

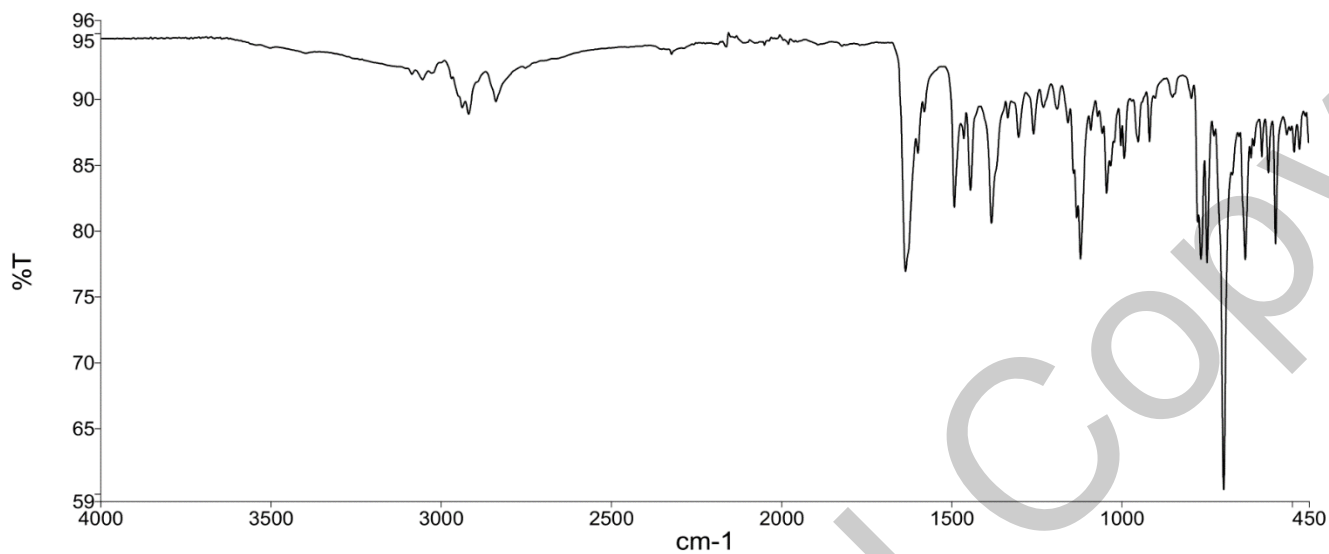
The signal of the Mass Spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.

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Ic. IR Spectrum

The infra-red spectrum of this material was analysed by Fourier-Transform Infrared Spectroscopy (FTIR) using in-house EM005.WI09.



The interpretation of the signals of the Fourier-Transform Infrared Spectrum is consistent with the structural formula.

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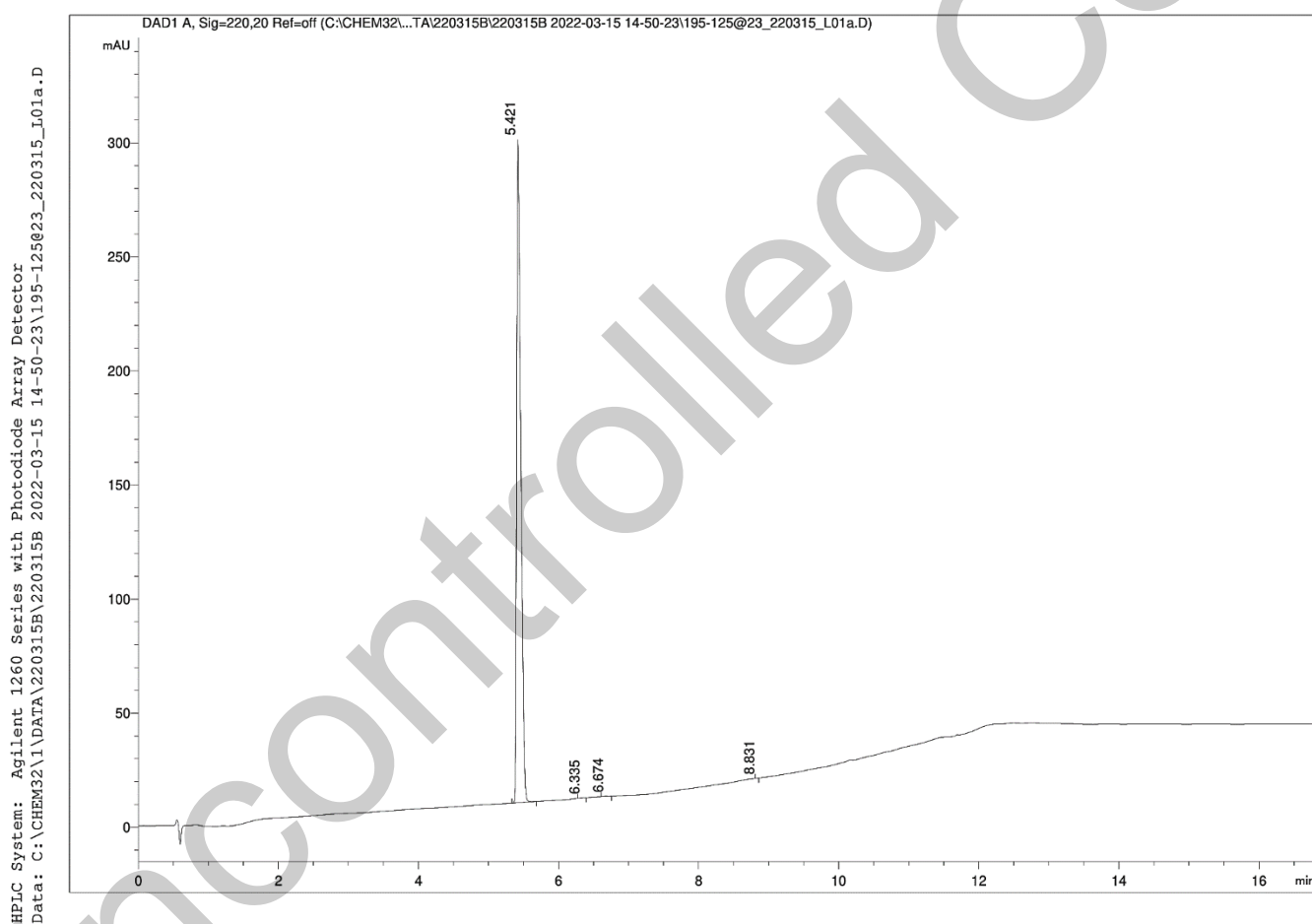
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II. Purity

The purity of this material was analysed by high performance liquid chromatography (HPLC) using in-house EM005.WI07.

HPLC Conditions:

Column	Conditions				Detector	Injector
Agilent Poroshell 120 EC-C18 4.6 x 50mm 2.7 micron	25°C				DAD 220nm	Auto 1.0 µL 0.75 mg/mL in 50% acetonitrile and 50% water (NO MODIFIERS)
	Time (min)	% Line A (Water + 0.1% (v/v) TFA)	% Line B (Acetonitrile + 0.1% (v/v) TFA)	Flow rate (mL/min)		
	0.00	75	25	1.0		
	6.00	51	49	1.0		
	10.60	5	95	1.0		
	15.60	5	95	1.0		
	16.60	75	25	1.0		
	19.60	75	25	1.0		



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Area Percent Report – Sorted by Signal

Peak Number	Retention Time (rounded)	Area	Area % (rounded)
1	5.42	1200.55	99.93
2	6.33	0.22	0.02
3	6.67	0.60	0.05
4	8.83	0.04	0.00
Totals			100 (rounded)

For the calculation the system peaks were ignored. The content of the analyte was determined as a ratio of the peak area of the analyte and the cumulative areas of the purities, added up to 100%.

Results:

Average 99.9% (average of 10 duplicate runs)

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III. Water Content

Method: Karl-Fischer titration using in-house EM005.WI04.

Results:

Average 0.9%

IV. Ash Content

Method: BP 2015 Ash (Appendix XI J) as per WS001/24163

Result:

Contains <0.1% ash.

V. Residual Solvents

Method: ¹H NMR

Result:

No significant impurities detected by ¹H NMR analysis.

VI. Final Result

Chromatographic purity (HPLC)	99.9%
Water content	0.9%
Ash content	<0.1%
Residual solvents	<0.1%
Purity*	99.0%

This purity is assessed to be 99.0%.

Product Reviewed By:

Jacob Heppell, PhD
Chemist

Product Released By:

Carol Worth, PhD
Quality Manager
Release Date: 22 March 2022

**NATA accreditation does not cover the performance of this service.*

The calculation of the purity follows the formula:

$$\text{Purity(\%)} = \frac{((\text{Chromatographic purity [HPLC]}) \times (100 - (\text{water content} + \text{ash content} + \text{volatile contents})))}{100}$$

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